

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

1-28. (Cancelled)

29. (Withdrawn-Currently Amended) A method for monitoring efficacy of a drug for treatment of mild osteoarthritis in a patient who has been diagnosed with mild osteoarthritis according to claim 38, comprising the steps of:

- (a) obtaining a sample from a said patient before treatment and a second sample from said patient after said treatment;
- (b) detecting the level of expression of the ~~biomarkers~~ genes TNFAIP6 and ~~TGFB1~~ TGFB1 TGFB1 in said first sample and said second sample; and
- (c) determining a difference in said level of expression of said ~~biomarker~~ genes in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of mild osteoarthritis in said patient.

30. (Withdrawn-Currently Amended) A method for monitoring the efficacy of a drug for treatment of moderate osteoarthritis in a patient who has been diagnosed with moderate osteoarthritis according to claim 46, comprising the steps of:

- (a) obtaining a sample from a said patient before treatment and a second sample from said patient after said treatment;
- (b) detecting the level of expression of each of the ~~biomarkers~~ genes TNFAIP6 and ~~TGFB1~~ TGFB1 TGFB1 in said first sample and said second sample; and
- (c) determining a difference in said level of expression of each said ~~biomarker~~ gene in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of moderate osteoarthritis in said patient.

31. (Withdrawn-Currently Amended) A method for monitoring efficacy of a drug for treatment of marked osteoarthritis in a patient who has been diagnosed with marked osteoarthritis according to claim 50, comprising the steps of:

- (a) obtaining a sample from a said patient before treatment and a second sample from said patient after said treatment;
- (b) detecting the level of expression of each of the biomarkers genes TNFAIP6 and ~~TGFB1~~ TGFBI in said first sample and said second sample; and
- (c) determining a difference in said level of expression of each said biomarker gene in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of marked osteoarthritis in said patient.

32. (Withdrawn-Currently Amended) A method for monitoring efficacy of a drug for treatment of severe osteoarthritis in a human patient who has been diagnosed with severe osteoarthritis according to claim 42, comprising the steps of:

- (a) obtaining a cartilage sample from a said human patient before treatment and a second cartilage sample from said patient after said treatment;
- (b) detecting the level of expression of each of the biomarkers genes TNFAIP6 and ~~TGFB1~~ TGFBI in said first sample and said second sample; and
- (c) determining a difference in said level of expression of each said biomarker gene in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of severe osteoarthritis in said patient.

33. (Withdrawn-Currently Amended) A method of identifying a therapeutic agent for the treatment of osteoarthritis, said method comprising:

- a) providing a cartilage sample from a human patient diagnosed with osteoarthritis;
- b) measuring the level of expression of each of the biomarkers genes TNFAIP6 and ~~TGFB1~~ TGFBI in the presence and the absence of said therapeutic agent; and
- c) comparing said level of expression measured in the presence of said therapeutic agent to said level of expression measured in the absence of said therapeutic agent, wherein a decrease

in the differential expression of each said biomarker gene is indicative of a therapeutic agent for the treatment of osteoarthritis.

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Currently Amended) A method of diagnosing mild osteoarthritis in ~~an~~ a human test individual, said method comprising:

for each gene of the set of genes consisting of TNFAIP6 and TGFBI,

(a) determining the level of expression of RNA ~~corresponding to biomarkers TNFAIP6 and TGFBI~~ encoded by said gene in a cartilage sample of said individual; and

(b) comparing the said level of expression of said RNA in said sample with the level of expression of RNA encoded by said gene ~~corresponding to said biomarkers in one or more control~~ cartilage samples, wherein said control samples are from individuals who have been diagnosed as not having osteoarthritis; ~~having either moderate osteoarthritis, marked osteoarthritis or severe osteoarthritis~~;

whereby a difference in between said level of expression of said RNA step (a) and said level of expression of said RNA in said control samples is indicative ~~or predictive~~ of mild osteoarthritis.

38. (Currently Amended) A method of diagnosing mild osteoarthritis in ~~an~~ a human test individual, said method comprising:

(a) for each gene of a set of genes, determining the a level of expression of RNA ~~corresponding to~~ encoded by said gene ~~one or more biomarkers~~ in a cartilage sample of said test individual;

(b) for each gene of said set of genes, comparing the level of expression of said RNA in said sample of said test individual with the a level of expression of RNA ~~corresponding~~

~~to said biomarkers encoded by said gene in one or more control cartilage samples wherein said control samples are from individuals who have been diagnosed as having either moderate osteoarthritis, marked osteoarthritis or severe osteoarthritis using the Marshall scoring system; obtained from each of: a population of human individuals not having osteoarthritis; a population of human individuals having mild osteoarthritis according to the Marshall scoring system; a population of human individuals having moderate osteoarthritis according to the Marshall scoring system; a population of human individuals having marked osteoarthritis according to the Marshall scoring system; and a population of human individuals having severe osteoarthritis according to the Marshall scoring system; whereby a difference in said level of expression of said RNA is indicative or predictive of mild osteoarthritis; and~~

(c) determining a difference in said levels of expression as between RNA encoded by said genes in said sample of said test individual and RNA encoded by said genes in said samples from said control populations such that said test individual is classified as having mild osteoarthritis;

thereby diagnosing said test individual as having mild osteoarthritis.

39. (Currently Amended) The method of claim 38, wherein said ~~one or more biomarkers genes~~ are selected from the group of genes identified in Figures 1-7.

40. (Currently Amended) The method of claim 38, wherein said ~~one or more biomarkers are biomarkers~~ set of genes consists of TNFAIP6 and TGFBI.

41. (Canceled)

42. (Currently Amended) A method of diagnosing severe osteoarthritis in ~~an~~ a human test individual, said method comprising

(a) for each gene of a set of genes, determining the level of expression of RNA corresponding to encoded by said gene ~~one or more biomarkers~~ in a cartilage sample of said test individual;

(b) for each gene of said set of genes, comparing the level of expression of said RNA in said sample of said test individual with the a level of expression of RNA corresponding to said biomarkers encoded by said gene in one or more control cartilage samples wherein said control samples are from individuals who have been diagnosed as having either mild osteoarthritis, marked osteoarthritis or moderate osteoarthritis using the Marshall scoring system obtained from each of: a population of human individuals not having osteoarthritis; a population of human individuals having mild osteoarthritis according to the Marshall scoring system; a population of human individuals having moderate osteoarthritis according to the Marshall scoring system; a population of human individuals having marked osteoarthritis according to the Marshall scoring system; and a population of human individuals having severe osteoarthritis according to the Marshall scoring system; whereby a difference in said level of expression of said RNA is indicative or predictive of severe osteoarthritis, and

(c) determining a difference in said levels of expression as between RNA encoded by said genes in said sample of said test individual and RNA encoded by said genes in said samples from said control populations such that said test individual is classified as having severe osteoarthritis;

thereby diagnosing said test individual as having severe osteoarthritis.

43. (Currently Amended) The method of claim 42, wherein said genes ~~one or more biomarkers~~ are selected from the group of genes identified in Figures 1-7.
44. (Currently Amended) The method of claim 42, wherein said ~~one or more biomarkers are biomarkers~~ set of genes consists of TNFAIP6 and ~~TGFB1~~ TGFBI.
45. (Cancelled)
46. (Currently Amended) A method of diagnosing moderate osteoarthritis in ~~an~~ a human test individual, said method comprising:

(a) for each gene of a set of genes, determining the a level of expression of RNA encoded by said gene corresponding to one or more biomarkers in a cartilage sample of said test individual;

(b) for each gene of said set of genes, comparing the said level of expression of said RNA in said sample of said test individual with the a level of expression of RNA corresponding to said biomarkers encoded by said gene in one or more control cartilage samples wherein said control samples are from individuals who have been diagnosed as having mild osteoarthritis, marked osteoarthritis or severe osteoarthritis using the Marshall scoring system; obtained from each of the following control populations: a population of human individuals not having osteoarthritis; a population of human individuals having mild osteoarthritis according to the Marshall scoring system; a population of human individuals having moderate osteoarthritis according to the Marshall scoring system; a population of human individuals having marked osteoarthritis according to the Marshall scoring system; and a population of human individuals having severe osteoarthritis according to the Marshall scoring system; whereby a difference in said level of expression of said RNA is indicative or predictive of moderate osteoarthritis. -and

(c) determining a difference in said levels of expression as between RNA encoded by said genes in said sample of said test individual and RNA encoded by said genes in said samples from said control populations such that said test individual is classified as having moderate osteoarthritis;

thereby diagnosing said test individual as having moderate osteoarthritis.

47. (Currently Amended) The method of claim 46, wherein said ~~one or more biomarkers~~ genes are selected from the group of genes identified in Figures 1-7.
48. (Currently Amended) The method of claim 46, wherein said ~~one or more biomarkers~~ are biomarkers set of genes consists of TNFAIP6 and TGFBI.
49. (Cancelled)

50. (Currently Amended) A method of diagnosing marked osteoarthritis in ~~an~~ a human test individual, said method comprising:

(a) for each gene of a set of genes, determining the a level of expression of RNA corresponding to one or more biomarkers encoded by said gene in a cartilage sample from said test individual;

(b) for each gene of said set of genes, comparing the said level of expression of said RNA in said sample of said test individual with the a level of expression of RNA corresponding to said biomarkers encoded by said gene in a control cartilage samples wherein said control sample is from one or more individuals who have been diagnosed as having either mild osteoarthritis, moderate osteoarthritis or severe osteoarthritis using the Marshall scoring system; obtained from each of the following control populations: a population of human individuals not having osteoarthritis; a population of human individuals having mild osteoarthritis according to the Marshall scoring system; a population of human individuals having moderate osteoarthritis according to the Marshall scoring system; a population of human individuals having marked osteoarthritis according to the Marshall scoring system; and a population of human individuals having severe osteoarthritis according to the Marshall scoring system; whereby a difference in said level of expression of said RNA is indicative or predictive of marked osteoarthritis. and

(c) determining a difference in said levels of expression as between RNA encoded by said genes in said sample of said test individual and RNA encoded by said genes in said samples from said control populations such that said test individual is classified as having marked osteoarthritis;

thereby diagnosing said test individual as having marked osteoarthritis.

51. (Currently Amended) The method of claim 50, wherein said ~~one or more biomarkers~~ genes are selected from ~~these~~ the group of genes identified in Figures 1-7.

52. (Currently Amended) The method of claim 50, wherein said ~~one or more biomarkers are~~ biomarkers set of genes consists of TNFAIP6 and TGFBI ~~TGFB1~~ TGFB1.

53. (Withdrawn-Currently Amended) A method for monitoring the efficacy of a drug for treatment of mild osteoarthritis in a human patient who has been diagnosed with mild osteoarthritis according to claim 37, further comprising the steps of:

(c) obtaining a cartilage sample from a said patient before treatment and a second cartilage sample from said patient after said treatment;

(d) detecting the level of expression of said ~~biomarkers~~ genes in said first sample and said second sample; and

(e) determining a difference in said level of expression of said biomarkers in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of mild osteoarthritis in said patient.

54. (Withdrawn-Currently Amended) A method for monitoring the efficacy of a drug for treatment of moderate osteoarthritis in a human patient who has been diagnosed with moderate osteoarthritis according to claim ~~45~~46, further comprising the steps of:

(d) obtaining a cartilage sample from a said human patient before treatment and a second sample from said patient after said treatment;

(e) detecting the level of expression of said biomarkers in said first sample and said second sample; and

(f) determining a difference in said level of expression of said biomarkers in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of moderate osteoarthritis in said patient.



55. (Withdrawn-Currently Amended) A method for monitoring the efficacy of a drug for treatment of marked osteoarthritis in a human patient who has been diagnosed with marked osteoarthritis according to claim 4950, comprising the steps of:

(d) obtaining a cartilage sample from a said patient before treatment and a second sample from said patient after said treatment;

(e) detecting the level of expression of said biomarkers in said first sample and said second sample; and

(f) determining a difference in said level of expression of said biomarkers in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of marked osteoarthritis in said patient.

56. (Withdrawn-Currently Amended) A method for monitoring the efficacy of a drug for treatment of severe osteoarthritis in a human patient who has been diagnosed with severe osteoarthritis according to claim 4241, further comprising the steps of:

(d) obtaining a cartilage sample from a said patient before treatment and a second cartilage sample from said patient after said treatment;

(e) detecting the level of expression of said biomarkers in said first sample and said second sample; and

(f) determining a difference in said level of expression of said biomarkers in said first sample as compared with said second sample, wherein said difference is indicative of the efficacy of said drug for said treatment of severe osteoarthritis in said patient.

57. (Withdrawn-Currently Amended) An isolated combination of biomarkers consisting essentially of the biomarkers TNFAIP6 and ~~TGFB1~~ TGFBI.

58. (Withdrawn-Currently Amended) An isolated combination of biomarkers consisting of the biomarkers TNFAIP6 and ~~TGFB1~~ TGFBI.

59. (Withdrawn-Currently Amended) A composition consisting essentially of the biomarkers TNFAIP6 and ~~TGFB1~~ TGFBI and a carrier.
60. (Withdrawn-Currently Amended) A composition comprising the biomarkers TNFAIP6 and ~~TGFB1~~ TGFBI and a carrier.
61. (Withdrawn-Currently Amended) A composition consisting of the biomarkers TNFAIP6 and ~~TGFB1~~ TGFBI and a carrier.
62. (New) The method of any one of claims 37, 38, 42, 46 and 50, wherein a cDNA or EST complementary to said RNA encoded by said gene is immobilized to a microarray.
63. (New) The method of any one of claims 37, 38, 42, 46 and 50, wherein said determining of said level of expression of said RNA is effected by hybridization of said RNA to a microarray.
64. (New) The method of any one of claims 37, 38, 42, 46 and 50, wherein said determining of said level of expression of said RNA is effected by real time TR-PCR.
65. (New) The method of claim 38, wherein said genes are selected from the group consisting of the genes identified in Figure 6a.
66. (New) The method of claim 38, wherein said genes are selected from the group consisting of the genes identified in Figure 7a.
67. (New) The method of claim 42, wherein said genes are selected from the group consisting of the genes identified in Figure 6d.
68. (New) The method of claim 42, wherein said genes are selected from the group consisting of the genes identified in Figure 7b.
69. (New) The method of claim 46, wherein said genes are selected from the group consisting of the genes identified in Figure 6b.

70. (New). The method of claim 50, wherein said genes are selected from the group consisting of the genes identified in Figure 6c.